REMARKS

F r the Examiner's convenience, attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

The above amendments are believed to place the subject application in condition for allowance or, alternatively, reduce issues for appeal. Therefore, entry of the amendments is proper.

Amendments to the Specification

The Specification was amended to update the status of the parent applications.

Comments regarding restriction requirement

Applicants reiterate that upon allowance of product claim 1, there should be rejoinder of "method of use" claims 12-13, in accordance with the Commissioner's Notice in the Official Gazette of March 26, 1996, entitled "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)." In addition, Applicants reiterate the impropriety of the "restriction requirement" between SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5 and SEQ ID NO:7. Applicants expressly reserve the right to petition the restriction requirement if the full scope of the claims is not considered.

Objection to the specification

The Examiner objected to the Specification for allegedly failing to provide proper antecedent basis for the claimed subject matter.

Originally filed claims 3 and 6 are believed to be fully supported by the instant application. Nevertheless, in order to expedite prosecution of this application, the language of claims 3 and 6 has been simplified, as suggested by the Examiner. Exemplary support for amended claims 3 and 6 can be found in the Specification at page 29, lines 1-8 and lines 21-26; and page 30, lines 17-23.

Accordingly, withdrawal of the objection to the Specification is requested.

Enablement rejection under 35 U.S.C. §112, first paragraph

Claims 1 and 9-11 were rejected under 35 U.S.C. §112, first paragraph, allegedly for lacking an enabling disclosure with respect to variants of SEQ ID NO:3. This rejection is also traversed.

It is believed that the Specification provides enablement commensurate in scope with originally filed claim 1. Nevertheless, in order to expedite prosecution of the subject application, claim 1 has been revised to recite antibodies which specifically bind polypeptides comprising a naturally-occurring amino acid sequence at least 90% identical to the full length of the sequence of SEQ ID NO:3, wherein said naturally-occurring amino acid sequence supports NADH dehydrogenase activity. An assay for monitoring NADH dehydrogenase is described in the Specification, for example, at page 52, lines 16-23. Applicants therefore respectfully request withdrawal of this rejection.

Rejections under 35 U.S.C. § 102 and § 103

Claims 1 and 4 were rejected under 35 U.S.C. § 102(b) as being anticipated by Bentlage et al. (Biochimica Biophysica Acta, 1234:63-73, 1995). In addition, a § 103 rejection of claims 1-11 was applied over the combination of Walker et al (J. Mol. Biol., 226:1051-1072, 1992) in view of Bentlage et al and Ramakrishnan et al (U.S. Patent No. 5, 817,310). These rejections are traversed.

These rejections appear to be based on the theory that polypeptides described in Bentlage et al. and Walker et al. share some similarity to SEQ ID NO:3 and, therefore, antibodies to the Bentlage and Walker proteins are relevant to antibodies within the scope of the claims of the present application.

To expedite prosecution of the subject application, claim 1 has been revised to recite antibodies which specially bind a polypeptide comprising, *inter alia*, the amino acid sequence of SEQ ID NO:1 or a polypeptide comprising, *inter alia*, a naturally-occurring amino acid sequence at least 90% identical to the full length of the sequence of SEQ ID NO:1 and which supports NADH dehydrogenase activity. None of the cited art discloses such a polypeptide or an antibody which specifically binds to such a polypeptide. Applicants expressly do not disclaim equivalents which would include antibodies that specifically bind to polypeptides which are insubstantially different from polypeptides comprising SEQ ID NO:1 or which are insubstantially different from

a polypeptide comprising a naturally-occurring amino acid sequence at least 90% identical to the full length of the sequence of SEQ ID NO:1 and which do or do not support NADH dehydrogenase activity. Applicants do not concede to the Patent Office position; Applicants are amending the claims solely to obtain expeditious allowance of the subject application.

For at least the above reasons, withdrawal of the §102 and §103 rejections is requested.

CONCLUSION

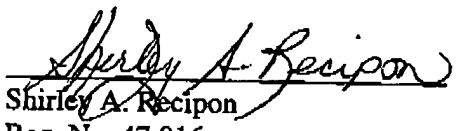
In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact Applicants' Attorney at (650) 855-0555.

Please charge Deposit Account No. **09-0108** in the amount of **$ 110.00** as set forth in the enclosed fee transmittal letter. If the USPTO determines that an additional fee is necessary, please charge any required fee to Deposit Account No. **09-0108.**

Respectfully submitted,
INCYTE GENOMICS, INC.

Date: 30 October 2002



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Docket No.: PF-0187-2 DIV

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

The paragraph beginning at page 1, line 3, has been amended as follows:

This is a **[DIVISIONAL]** divisional of Serial No.09/151,412, filed on September 10, 1998, issued on June 4, 2002, as U.S. Patent No. 6,399,345, entitled SUBUNITS OF NADH DEHYDROGENASE, which is a divisional of U.S. Serial No. 08/785,065, filed on January 17, 1997, issued on September 29, 1998, as U.S. Patent No. 5, 814,451, entitled [NOVEL] SUBUNITS OF NADH DEHYDROGENASE.

IN THE CLAIMS:

Claim 14 has been canceled.

Claims 1, 3 and 6 have been amended as follows:

1. **(Three Time Amended)** An isolated antibody which specifically binds to a polypeptide [comprising an amino acid sequence] selected from the group consisting of:

a) a polypeptide comprising the [an] amino acid sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, or SEQ ID NO:7, and

b) a polypeptide comprising a naturally-occurring amino acid sequence [having] at least 90% identical [sequence identity] to the full length of the sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, or SEQ ID NO:7, [and] wherein said naturally-occurring amino acid sequence supports NADH dehydrogenase activity

[c) an immunogenic fragment of a polypeptide having the amino acid sequence of SEQ ID NO:1, SEQ ID NO:5, or SEQ ID NO:7].

3. **(Once Amended)** A method of preparing a polyclonal antibody with the specificity of the antibody of claim 1 comprising:

a) immunizing an animal with the polypeptide of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, or SEQ ID NO:7, or an antigenically-effective fragment thereof under

conditions to elicit an antibody response; and

b) [isolating animal antibodies; and

c)] screening [the isolated] for antibodies with the polypeptide thereby identifying a polyclonal antibody which binds specifically to the polypeptide of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, or SEQ ID NO:7.

6. **(Twice Amended)** A method of making a monoclonal antibody with the specificity of the antibody of claim 1 comprising:

a) [immunizing an animal with] using the polypeptide of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, or SEQ ID NO:7, or an antigenically-effective fragment thereof, [under conditions to elicit an antibody response;] to make antibody-producing hybridoma cells; and

b) [isolating antibody producing cells from the animal;

c) fusing the antibody producing cells with immortalized cells in culture to form monoclonal antibody-producing hybridoma cells;

d) culturing the hybridoma cells; and

e) isolating from the culture] screening for antibodies with the polypeptide, thereby identifying a monoclonal antibody which binds specifically to the polypeptide of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, or SEQ ID NO:7.